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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,825	01/30/2002	Roderick John Scott	0623.1160001/LBB/GLL	2437
26191	7590	06/07/2005	EXAMINER	
FISH & RICHARDSON P.C. PO BOX 1022 MINNEAPOLIS, MN 55440-1022			BAUM, STUART F	
			ART UNIT	PAPER NUMBER
			1638	

DATE MAILED: 06/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/058,825	Applicant(s) SCOTT, RODERICK JOHN	
	Examiner Stuart F. Baum	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 25 February 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 20,21,62-67,69,71-74,76-78 and 80-82 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20,21,62-67,69,71-74,76-78 and 80-82 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>2/25/2005</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. The amendment filed 2/25/2005 has been entered.  
Claims 1-19, 22-61, 68, 70, 75 and 79 have been canceled.
2. Claims 20-21, 62-67, 69, 71-74, 76-78 and 80-82 are pending and are examined in the present office action.
3. Rejections and objections not set forth below are withdrawn.
4. The text of those sections of Title 35, U.S. Code not included in this office action can be found in a prior office action.

### ***Indefiniteness***

5. Claims 20-21, 62-67, 69, 71-74, 76-78, 80-82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection includes dependent claims.

Claims 20 is indefinite and claim 62 remains indefinite in the recitation "Met1". The sole designation of a nucleic acid sequence by "Met1" is arbitrary and creates ambiguity in the claims. For example, the nucleic acid sequence in this application could be designated by some other arbitrary means, or the assignment of said name could be arbitrarily changed to designate a different nucleic acid sequence. If either event occurs, one's ability to determine the metes and bounds of the claim would be impaired. See *In re Hammack*, 427 F.2d 1378, 1382; 166 USPQ 204, 208 (CCPA 1970). Amendment of the claim to refer to a specific SEQ ID NO would obviate this rejection. This rejection is maintained for the reasons of record set forth in the Official action mailed 10/25/2004. Applicant's arguments filed 2/25/2005 have been fully considered but they are not persuasive.

Applicants contend that the instant specification describes MET1 as a methylation enzyme from *Arabidopsis* and that the specification references Finnegan et al and Ronemus et al for the MET1 gene (page 8, 2nd paragraph). Applicants contend that these references explain that MET1 refers to the *Arabidopsis* cytosine methyltransferase gene that was published under the Genbank number L10692. In addition, Figure 6 of the instant application depicts the MET1 gene. Lastly, Applicants contend that the metes and bounds of the claimed subject matter would be recognized by one of skill in the art.

The Office contends that Applicants have not explicitly defined "MET1" to denote a specific nucleic acid sequence. Figure 6 in the instant application is only a schematic of a MET1 amino acid encoding nucleic acid molecule showing relative positions of restriction enzyme cleavage sites. Applicants are relying on the prior art references to define "MET1" but Applicants have not explicitly indicated that the "MET1" nucleic acid sequence is set forth in a specific accession number. In fact, Applicants also define MET1 to also include ribozyme sequences (See claim 72, 73 and 74). As discussed above, the use of term "MET1" is arbitrary and creates ambiguity in the claims.

### ***Written Description***

6. Claims 20-21, 62-67, 69, 71-74, 76-78 and 80-82 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained

for the reasons of record set forth in the Official action mailed 10/25/2004. Applicant's arguments filed 2/25/2005 have been fully considered but they are not persuasive.

Applicants contend that the instant application identifies *Arabidopsis* MET1 as an *Arabidopsis* gene with a known sequence as evidenced by the published literature and Applicants disclose in Figure 6 is a schematic description of the structure of MET1. Applicants also disclose primers that amplify MET1. Applicants contend that all of these descriptions is sufficient to identify *Arabidopsis* MET1 to one of skill in the art (page 9, 4th full paragraph). Applicants also disclose other methylating enzymes of which MET1 is included. Applicants disclose that accession number C10692 is incorrect and should be listed as L10692 (paragraph bridging pages 9 and 10). Applicants also contend that the application describes orthologs of MET1 that can be used in the methods therein, including *Z. mays* MET1, for which Applicants disclose Genbank accession No. AF063403 (page 10, 1st full paragraph). Applicants contend that the specification describes a wide variety of nucleic acid molecules that can be used in the methods to reduce methylation in plants. For example, antisense constructs, sense nucleic acids, partial sense nucleic acids and ribozymes. Applicants contend that because MET1 is known, Applicants are in possession of all such types of nucleic acids as they pertain to MET1 (page 10, bottom paragraph). Applicants contend that the specification describes ribozymes of MET1 (page 11, top paragraph).

The Office contends that Applicants are claiming a genus of sequences because of the recitation "partial or full length *Arabidopsis* MET1" or "partial or full length *Z. mays* sequences" but Applicants have not disclosed a representative number of *Arabidopsis* MET1 or *Z. mays* sequences identified by SEQ ID NO, nor have Applicants disclosed any partial sequences that

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have the same function as the full length sequence wherein the introduced nucleic acid is effective for down-regulating one or more methylating enzymes in any plant. Applicants have not disclosed essential elements of the disclosed genus. Applicants have also not disclosed any MET1 sequences that are ribozyme sequences or that encode ribozymes. The Office contends that Applicants are not in possession of the genus of MET1 sequences to which Applicants methods are drawn.

### ***Scope of Enablement***

7. Claims 20-21, 62-67, 69, 71-74, 76-78 and 80-82 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for increasing the amount of endosperm in a seed comprising a construct comprising a MET1 cDNA operably linked to any promoter that expresses in the male or female gametophyte in antisense orientation, wherein the MET1 cDNA is isolated by RT-PCR from Arabidopsis using the primers MET1F of SEQ ID NO:5 and MET1R of SEQ ID NO:6 and plant transformation therewith, does not reasonably provide enablement for claims broadly drawn to a method of modifying the endosperm comprising down-regulating any DNA methylating enzyme using any nucleic acid sequence, wherein the nucleic acid sequence encodes any Met1 protein or encodes a *Z. mays* Met1 orthologue, or any ribozyme or a ribozyme to a *Z. mays* orthologue, or wherein the nucleic acid is a partial or full length sense copy encoding a DNA methylating enzyme wherein the methylating enzyme is a *Z. mays* orthologue to Met1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is maintained

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for the reasons of record set forth in the Official action mailed 10/25/2004. Applicant's arguments filed 2/25/2005 have been fully considered but they are not persuasive.

Applicants contend that the specification provides guidance for one of skill in the art to make and use the claimed methods for modifying endosperm (page 13, 1<sup>st</sup> full paragraph). Applicants contend that the specification provides working examples that exemplify the claimed methods (page 13, 2<sup>nd</sup> full paragraph).

The Office contends that the specification provides guidance for a plant transformed with a nucleic acid that is isolated from Arabidopsis using the method as discussed above. Applicants have not provided guidance for partial sequences of any Arabidopsis or Z. mays MET1 sequence or for any MET1 sequence that is a ribozyme sequence or that encodes any ribozyme. Given the unpredictability as stated in the office action mailed on 10/25/2004, undue trial and error experimentation would be required by one of skill in the art to practice the claimed invention.

Applicants contend that the Jacobsen et al reference is directed toward hypermethylation gene silencing of the SUPERMAN gene and that this gene is not the subject matter of the instant claims. Applicants contend that Jacobsen et al do not assert that antisense is unpredictable, nor that the MET1 gene is unpredictable (page 14, 1<sup>st</sup> full paragraph).

The Office contends that the Jacobsen et al reference was used as an example of unpredictability because Jacobsen et al used the same nucleic acid as Applicants' claimed method and the result was that the SUPERMAN gene became hypermethylated instead of hypomethylated, as is the outcome in Applicants' method. Therefore, the Jacobsen et al reference does in fact teach unpredictability in using Applicants' claimed method.

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Applicants contend that all aspects of the claimed invention need not be disclosed what is well-known in the art. Applicants contend that one of skill in the art was very familiar with cloning by hybridization and PCR methods of orthologs of genes (page 14, 2<sup>nd</sup> full paragraph).

The Office contends that the methods are not the issue. The issue is that Applicants are claiming partial sequences of Arabidopsis and Z. mays MET1 sequences used in sense or antisense orientation, and also ribozymes. Applicants have not disclosed which partial sequences, or which sequences encode ribozymes, that can be used in Applicants method. Undue trial and error experimentation would be required by one of skill in the art to identify, isolate and test the multitude of non-exemplified sequences.

Applicants contend that the Fourgoux-Nicol reference does not teach unpredictability and that said reference does not has no mention of degenerate primers. Applicants also contend that Applicants' method is not limited to any particular method of isolating orthologs (paragraph bridging pages 14-15).

The Office contends that the Fourgoux-Nicol reference teaches unpredictability of hybridization techniques. The Office acknowledges that Applicants' methods are not limited to using degenerate primers as a method of isolating orthologs, but, Applicants' methods encompass degenerate primers, and as such, the use of the Fourgoux-Nicol reference is on point for teaching unpredictability.

Applicants contend that the Gutterson et al reference teach enablement of the claims from the instant application (page 15, middle paragraph).

The Office contends that the Gutterson et al reference may teach enablement for some aspects of co-suppression, but said reference also teaches unpredictability of co-suppression.



Applicants contend that the Emery et al reference does not teach unpredictability but rather teach that altering one base of a nucleic acid will interfere with binding of said nucleic acid with the target sequence (paragraph bridging pages 15-16).

The Office contends that the Emery et al reference was cited in support of unpredictability when using degenerate DNA sequences for co-suppression or antisense suppression. The reference demonstrates that when a single base is changed in comparison to the target sequence, the two sequences will not bind together. The result is there will not be a suppression of gene expression for the target sequence.

Applicants contend that the Mazzolini et al reference was published 7 years before the filing date of the instant application. Hence it does not represent the state-of-the-art at the time of filing (page 16, bottom paragraph).

In response to applicant's argument based upon the age of the references, contentions that the reference is old is not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

### ***Obviousness***

8. Claims 20-21, 64-65, 77-78 and 81 remain rejected under 35 U.S.C. 102(b) as being anticipated by Ronemus et al (1996, Science 273 (2 August):654-657). This rejection is maintained for the reasons of record set forth in the Official action mailed 10/25/2004. Applicant's arguments filed 2/25/2005 have been fully considered but they are not persuasive.

Applicants contend the Ronemus et al reference does not disclose methods of producing modified endosperm. Applicants contend the cited reference does not disclose any nucleic acid constructs that direct expression in female germ line cells (page 17, bottom paragraph). Applicants contend Ronemus et al do not disclose methods that include the step of directing expression of MET1 in female germ line cells. Applicants contend that the term “directing expression in female germ line cells” relates to the restricted expression in female germ line cells, not generalized expression in other cells such as the other (male) gamete tissue (page 18, middle paragraph). Applicants contend that Ronemus et al do not mention modified endosperm, nor any modified endosperm phenotypes at al (page 19).

The office contends that the Ronemus et al reference teach the claimed invention. See *Integra LifeSciences I Ltd. V. Merck KGaA* 50 USPQ2d 1846, 1850 (DC SCalif 1999), which teaches that where the prior art teaches all of the required steps to practice the claimed method and no additional manipulation is required to produce the claimed result, then the prior art anticipates the claimed method. It is an inherent feature of the 35S promoter to expression in all tissues, because it is a constitutive promoter. All tissues include expression in female germ line cells. Applicants contend that the term “directing expression in female germ line cells” relates to the restricted expression in female germ line cells, not generalized expression in other cells such as the other (male) gamete tissue. But the Office contends Applicant is arguing limitations not stated in the claims. Applicants’ arguments are not commensurate in scope with the claimed invention and although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

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9. No claims are allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Stuart F. Baum Ph.D.  
Patent Examiner  
Art Unit 1638  
May 23, 2005

A handwritten signature in black ink, appearing to read "Amy Nelson", with a stylized flourish at the end.

AMY J. NELSON, PH.D  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600